ACTA PÆDIATRICA
NURTURING THE CHILD

Accurate neonatal heart rate monitoring using a new wireless, cap mounted device

Journal:	*Acta Paediatrica*
Manuscript ID	SPAE-2020-0096.R2
Manuscript Type:	Regular Article
Date Submitted by the Author:	05-Apr-2020
Complete List of Authors:	Henry, Caroline; University of Nottingham, Division of Child Health, Obstetrics & Gynaecology Shipley, Lara; University of Nottingham, Division of Child Health, Obstetrics & Gynaecology Ward, Carole; University of Nottingham, Division of Child Health, Obstetrics & Gynaecology Mirahmadi, Siavash; University of Nottingham Faculty of Engineering Liu, Chong; University of Nottingham Faculty of Engineering Morgan, Steve; University of Nottingham Faculty of Engineering Crowe, John; University of Nottingham Faculty of Engineering Carpenter, James; Surepulse Medical Ltd Hayes-Gill, Barrie; University of Nottingham Faculty of Engineering Sharkey, Don; University of Nottingham School of Medicine, Academic Child Health
Keywords:	heart rate monitoring, infant, newborn, photoplethysmography, neonatal resuscitation, technologies, wireless
Note: The following files were submitted by the author for peer review, but cannot be converted to PDF. You must view these files (e.g. movies) online.	
fhPPG video example.mp4	

TITLE

Accurate neonatal heart rate monitoring using a new wireless, cap mounted device

Caroline Henry[1], Lara Shipley[1], Carole Ward[1], Siavash Mirahmadi[2], Chong Liu[2], Steve Morgan[2], John Crowe[2], James Carpenter[3], Barrie Hayes-Gill[2], Don Sharkey[1]

[1]Division of Child Health, Obstetrics & Gynaecology, University of Nottingham, UK; [2]Faculty of Engineering, University of Nottingham, UK; [3]SurePulse Limited, Nottingham, UK

Short title: Neonatal heart rate monitoring

Corresponding author: Don Sharkey, Division of Child Health, Obstetrics & Gynaecology University of Nottingham, Queen's Medical Centre Campus, Derby Road, Nottingham, UK NG7 2UH. Tel 01158230602

ABSTRACT

Aim: A device for newborn heart rate (HR) monitoring at birth that is compatible with delayed cord clamping and minimises hypothermia risk could have advantages over current approaches. We evaluated a wireless, cap-mounted device (fhPPG) for monitoring neonatal HR. ***Methods***: 52 infants on the Neonatal Intensive Care Unit (NICU) and immediately following birth by elective caesarean section (ECS) were recruited. HR was monitored by electrocardiogram (ECG), pulse oximetry (PO) and the fhPPG device. Success rate, accuracy and time to output HR were compared with ECG as the gold standard. Standardised simulated data assessed the fhPPG algorithm accuracy. ***Results***: Compared to ECG HR, the median bias (and 95% limits of agreement) for the NICU were fhPPG -0.6 (-5.6, 4.9) vs PO -0.3 (-6.3, 6.2) bpm, and ECS phase fhPPG -0.5 (-8.7, 7.7) vs PO -0.1 (-7.6, 7.1) bpm. In both settings, fhPPG and PO correlated with paired-ECG HRs (both R^2=0.89). The fhPPG HR algorithm during simulations demonstrated a near-linear correlation (n=1266, R^2=0.99).

Conclusion: Monitoring infants in the NICU and following ECS using a wireless, cap mounted device provides accurate HR measurements. This alternative approach could confer advantages compared with current methods of HR assessment and warrants further evaluation at birth.

Keywords

Heart Rate; Infant, Newborn; Photoplethysmography; Resuscitation; Technologies, wireless

KEY NOTES

- Wireless continuous heart rate (HR) monitoring of infants using a cap (fhPPG) could be beneficial during delayed cord clamping
- Using electrocardiography as a gold standard, the fhPPG had similar bias and 95% limits of agreement as pulse oximetry on the Neonatal Intensive Care Unit and immediately after birth by caesarean section. There was close correlation to paired-ECG HRs
- Using standardised simulated HR data, the fhPPG algorithm demonstrated near-linear correlation
- The fhPPG is an accurate alternative to current methods of HR monitoring

INTRODUCTION

Approximately 10% of newborns require assistance at birth to establish breathing with 3% needing more sustained stabilisation or resuscitation.(1) Preterm infants often require more advanced stabilisation or resuscitation whilst avoiding hypothermia, known to increase mortality.(2, 3) Heart rate (HR) is the most sensitive predictor of the infant's clinical status and the efficacy of any interventions, and international guidelines suggest the electrocardiogram (ECG) may be used in the delivery room to monitor it.(4) However, electrode application can be difficult, ECG monitors are not always available and electrical cardiac activity may not always equate to effective cardiac output.(5, 6) Pulse oximetry (PO) is widely used on neonatal intensive care units (NICUs) but uptake in the delivery room is not universal (7) potentially because of the delay of a few minutes to obtain a reliable HR after birth due to poor peripheral perfusion and motion.(8) This could explain why PO underestimates HR when compared to ECG during the first minutes of life.(9, 10)

Delayed cord clamping (DCC) for term infants is widely practiced and could become more common for preterm infants but there is a need to better monitor these babies during this transition to maximise the benefits of DCC whilst avoiding any adverse effects of delayed resuscitation.(11, 12) Maximising placental transfusion requires the attending team to be confident of the baby's condition including an acceptable HR and avoidance of hypothermia. A non-intrusive, wireless, easy to apply HR monitoring system, which avoids the risk of hypothermia, could be advantageous in this setting.

We have previously described a prototype wired, forehead mounted sensor studied in NICU patients that utilises reflectance mode green light photoplethysmography (PPG) to measure HR.(13) This has the advantages that this wavelength of light (525 nm) is optimised for reflection mode detection of blood flow and captures this at the forehead where brain perfusion shares arterial pathways via the carotid artery and so is less susceptible to poor peripheral perfusion.(14, 15) This original device was held in place on the forehead by a spun bond laminate headband and successfully demonstrated that HR measurement by this method was feasible but had a Bland-Altman limit of agreement (LOA) of up to ±12bpm. In addition, it was not compatible with current neonatal care due to its inability to accommodate endotracheal tube and CPAP attachments. Furthermore, the relatively large sensor (22 mm diameter), large electronic circuit boards and the presence of cumbersome wiring were less suited for bedside stabilisation of preterm infants during DCC.

This device has now been substantially modified (Supplemental video and images) in terms of its practicality and several major modifications have taken place including:

i) A T-shape cap compatible with respiratory equipment fittings

ii) A miniaturised and ruggedized sensor (10 mm diameter)

iii) Bluetooth (BT) wireless connection removing the need for trailing wires

The primary aim of this study was to assess, via a clinical trial, the accuracy and reliability of this new cap mounted newborn HR device the SurePulse VS (fhPPG) (SurePulse Medical Ltd, Nottingham, UK). The study was designed to satisfy the regulatory requirements of the CE Medical Devices Directive 93/42 and its 2007 amendment for measuring HR compared to PO, with ECG as a gold standard. A secondary aim was to investigate acquisition time.

MATERIALS AND METHODS

Study Population

This prospective observational study was conducted at the Nottingham University Hospitals NHS Trust, UK following ethical approval (NHS Health Research Authority Yorkshire & The Humber – Sheffield Research Ethics Committee 15/YH/0522). Informed parental consent was obtained prior to infants being enrolled in the study and evaluations were performed in the NICU and on babies born by elective caesarean section (ECS). For the NICU phase, infants were included if they were >22 weeks gestation, required HR monitoring and were deemed clinically stable by the attending team. Inclusion criteria for the ECS phase were infants ≥37 weeks gestation with no obvious requirement for resuscitation, based on antenatal history, and delivered by planned caesarean section.

Study Design

There were two phases to this study, the NICU and ECS. On the NICU, an appropriately sized fhPPG cap was fitted to the infant's head and connected wirelessly to a bespoke synchronised data-logging system via the inbuilt wireless BT module. As part of their routine care, infants had 3 neonatal ECG monitoring electrodes (PD50-F4C, SKINTACT, Leonhard Lang GmbH, Innsbruck, Austria) attached and connected to a CARESCAPE Monitor B450 (General Electric Healthcare, Illinois, United States) with Masimo SET® for SpO2 (Masimo, California, United States). A transmission mode PO sensor (LNCS Neo, Masimo, California, United States) was attached to the wrist of the right hand and connected to the same monitor. An in-house designed system using LabVIEW 2014 (National Instruments, Texas, United States) simultaneously collected synchronised data from all devices and displayed waveforms from each device in real time on a laptop (Lenovo Y50 20378, Lenovo Group Ltd, Hong Kong). In keeping with normal practice, if any device presented a poor signal output the electrodes or optical sensors (head or wrist) were repositioned. Up to 30 minutes of raw physiological data were collected with the infant in their cot or incubator.

During the ECS phase, the same monitoring system described above was deployed. Following birth, the baby was shown to parents before being placed on the resuscitaire. All monitoring equipment was attached in the same sequence for each patient by the research team. The fhPPG cap was fitted, ECG leads attached and a PO sensor attached to the wrist of the right hand(16-18) and raw data collected for up to 20 minutes.

The B450 monitor generates HR data which provides ECG and PO values every 5 seconds. All fhPPG HR data extracted were averaged over the same 5 second window for direct comparison.

Slow and rapidly changing HRs can be unpredictable in the NICU and ECS settings. To ensure the fhPPG HR algorithm can effectively extract a wide range of rapidly changing HRs, as experienced during newborn care, we subjected the algorithm to simulated HR data covering 25 to 250 bpm using the Japanese Industrial Standard (JIS T 1303:2005, revised 2018).(19) Although the JIS T is designed for testing fetal heart rate monitors, it appropriately models newborns as the HR baseline and variation are similar to those of the fetus.(20) A simulated PPG signal was input across the JIS T range of HRs, the algorithm's performance tracked and linear regression applied to evaluate the overall performance.

Data Analysis

HR data from either PO or fhPPG were excluded if there was no ECG (the gold standard) HR comparator, a protocol violation occurred or a device was detached from the patient. To ensure good quality gold standard data, erroneous ECG HR data, as previously observed,(13) were excluded if there was no discernible QRS complexes or there had been an algorithm drop out. If the ECG HR value deviated by >20% from the other test devices (PO and/or fhPPG), the RR interval on the raw ECG trace corresponding to that time point was manually checked and excluded if the manual ECG HR check deviated from the reported ECG HR by >10%.

The success rate was calculated as the percentage of time during which the device in question was attached to the patient and reporting a HR once all three devices were simultaneously outputting a valid HR.

Comparison of the HR accuracy (fhPPG and PO) with the gold standard (ECG) utilised three methods: 1) Positive Percent Agreement (PPA) which is the percentage of time the test device generated a valid HR within 10% of the paired ECG HR,(21) 2) modified Bland-Altman plots to correct for multiple measurements and it's limits of agreement (LOA),(22, 23) and 3) Root-Mean-Square Error (RMSE) calculated between paired HRs (fhPPG vs ECG, and PO vs ECG). HR output time for each device is the time taken from completion of its attachment to the display of a HR.

Analyses were performed using GraphPad Prism 7.01 (GraphPad, California, USA). Continuous variables were tested for normality using the Kolmogorov-Smirnov test. Data were presented as mean (SD), median (range), or median (IQR) where appropriate. Non-parametric data were compared using the Wilcoxon signed rank test and between groups were compared using Friedman's test with a Dunn's correction for multiple comparisons. The study was registered at Clinicaltrials.gov NCT 02701920.

RESULTS

A convenience sample of 60 infants were recruited (NICU = 40, ECS = 20) when researchers were available. Six infants were excluded from the NICU phase and two from the ECS phase due to ECG data not being stored or corrupted leading to data loss and misalignment. The patient demographics can be seen in Table 1.

Success Rate

During the NICU phase, the median ECG success rate was 100% (IQR, 100-100, n=12967), PO was 100% (IQR, 99.1-100, n=12688) and fhPPG was 98.7% (IQR, 93.9-100, n=11501). During the ECS phase, the median ECG success rate was 96.2% (IQR, 91.9-100, n=2039), PO was 98.1% (IQR, 89.5-100, n=1903) and fhPPG was 94.1% (IQR, 84.1- 98.4, n=1805).

Accuracy of devices

During the NICU phase, the median PPAs were similar for fhPPG (99.6%; IQR 99.0-100, n=11353) and PO (99.4%; IQR 99.0-100, n=12249). During the ECS phase, the median

PPAs were again similar for fhPPG (98.6%; IQR 96.4-100, n=1584) and PO (98.7%; IQR 97.2-100, n=1684). Device comparison to the gold standard was also determined using both Bland-Altman plots (Table 2) and RMSE (Table 2 and Figure 1).

Linear regression of all pooled paired HRs demonstrated PO and fhPPG had similar goodness of fit with both having an R^2=0.89 (Figure 2). In five babies, the ECG measured a HR<100 bpm. For these, there were 23 paired values with the PO of which two reported a HR>100 bpm and for the fhPPG there were 13 paired values with two reporting a HR>100 bpm, on both occasions the fhPPG output was identified as a poor signal triggering a warning to the user.

Algorithm simulation

Simulated PPG data were applied as described across a range of HRs and with varying rates of change as defined by JIS T (Figure 3). The fhPPG algorithm demonstrated excellent correlation with the simulated HR (Figure 4).

Heart rate output time

Median time for HR output was similar for all three devices during the ECS phase. For ECG this was 24.5s (IQR 14.2-31.2), fhPPG 35.5s (IQR 16.7-53.7) and PO 24.5s (IQR 13.5-53.5) with no statistical significance between any of the devices.

DISCUSSION

We aimed to establish the accuracy and reliability of a new wireless, cap mounted HR monitoring device (fhPPG) in the neonatal setting and compare this to the HR obtained from PO. The fhPPG device provided accurate and reliable HR data compared to current predicate devices generating a median RMSE of 2.8 bpm compared to 3.3 bpm for PO in the NICU. In the ECS phase at birth, median RMSE values of 4.1 bpm and 3.7 bpm were obtained for the fhPPG and PO devices respectively. Time to output a HR after placement in the delivery room was similar across all three devices.

All devices provided similar success rates when outputting a HR. During the NICU phase, the fhPPG device had fewer data points because of the requirement to remove and replace the device for safety checks as required by the Ethics panel. The high ECG success rate reflects the use of electrodes that were already in place for normal neonatal care and, unlike the fhPPG device, were not removed and re-sited for safety and acquisition time purposes.

Accuracy, as measured by PPA, Bland-Altman and RMSE demonstrated the fhPPG device was similar to the PO in both settings. The measures of variance for each of these measures were within clinically acceptable limits, both optical devices providing accurate data when compared to the ECG that detects electrical activity. This requires the algorithms to respond in a timely fashion to rapid changes in HR, a key requirement of any device in these settings. For PO in the NICU, Singh et al (2008) had demonstrated the Bland-Altman LOA of ±12 bpm.(24) In our study, the PO performed much better in the NICU and ECS groups. For the new fhPPG device, accuracy in the NICU has improved to approximately ±5 bpm from the previous iteration with LOAs of up to ±12 bpm.(13) This improved accuracy remained for the fhPPG device during the ECS phase with LOAs of approximately ±8 bpm. PO has been studied in the delivery room across a range of gestational ages. Kamlin et al's study were mostly mature infants, with a mean gestational age of 35 weeks, and the majority (65%) did not require any intervention. The Bland-Altman demonstrated a mean difference of -2 bpm and LOA of ±26 bpm. The results for both PO and fhPPG in the present study were significantly better although the groups were not entirely comparable with only infants ≥37 weeks gestation recruited at birth in the ECS group. The additional measures of HR accuracy also add confidence that the fhPPG device performs as well as current devices with a PPA of approximately 99%, in the NICU and ECS phase, and an RMSE 3-4 bpm. Furthermore, both the PO and fhPPG devices produced high correlations with an R^2=0.89 for goodness-of-fit compared to ECG HR. For the ECS phase, these data are reassuring given the vigorous nature of the babies at birth and the significant motion artefact introduced.

It is essential that any newborn HR monitoring device is able to detect low rates, particularly those below 100bpm. The majority of babies in this study were stable with limited HR variability so limiting the number of HRs <100bpm. Use of the JIS T methodology allowed us to test the software algorithm to rapidly changing simulated HRs across the typical newborn range. The fhPPG algorithm was able to track the HRs quickly and accurately with an R^2=0.994. This strong correlation supports the accuracy of the device's software based on simulation data but the whole system requires real-world evaluation with infants undergoing resuscitation or stabilisation.

The secondary aim of this study was to explore the acquisition time of the new device, as it is essential for fast delivery of information to the attending team to allow correct management of the baby. Output of the HR at birth for all devices was similar although more babies in the study would be required to confirm this persisted or identify any differences. ECG measures electrical activity and has been shown to acquire a HR quicker than pulse oximeters, possibly reflecting delayed acquisition from early cutaneous perfusion increasing in the first few minutes of life. The fhPPG device uses green light to measure HR, but also has red and infrared light that are optimised for oxygen saturation measurement and used by POs to measure HR. Green light is better suited to detecting pulsatile blood flow (13) so potentially optimising HR estimation particularly during low perfusion states. The sequence of device attachment after birth was fhPPG, ECG and PO respectively, potentially disadvantaging the fhPPG device as it was placed earlier during the transition period. Whilst fast detection of electrical activity of the heart is useful, when cardiac output is poor or non-existent(5, 6) there could be advantages to having a parallel optical sensor that is able to detect blood flow and hence confirm the electrical activity is associated with cardiac output. Any potential benefits of a centrally placed, green light optical sensor, i.e. fhPPG which detects blood flow from the forehead sharing a common central arterial blood supply to the brain, compared to a peripherally sited transmission mode device requires further evaluation in larger number of patients including preterm infants.

The main limitation of the present study is the low number of HRs below 100, reflecting the nature of the population who were stable NICU patients or ECS term babies born following uncomplicated pregnancies. There were fewer paired ECG and fhPPG values <100bpm, compared to the PO, due to sensor repositioning as the signal had been identified as poor. We mitigated against low HRs by using the JIS T methodology fully exercising the software algorithm to create HR values over the range 25-250 bpm confirming successful algorithm functionality. However, additional studies are required to establish this in compromised newborns, especially those with HRs<100 bpm, where the HR variability changes frequently and a larger number of preterm infants.

CONCLUSION

With the increasing use of DCC the development of a wireless, continuous HR monitor that aligns with the normal care pathway, including placement of a cap with attachment for respiratory equipment, could better support transitioning of newborn babies and audit interventions.(25) Confidence in such a device could allow monitoring of the newborn and aid decisions around when to clamp the cord and instigate any stabilisation or additional resuscitation steps. fhPPG operates in reflectance mode allowing detection of a PPG signal on many parts of the body. The forehead allows inclusion in a cap, normally applied to keep the baby warm, and could potentially improve reliability during low perfusion states with a shared carotid artery blood supply to the brain.(13) The wireless design avoids multiple trailing wires that could become accidentally detached during bedside care with DCC. This device provides healthcare professionals with an accurate alternative to current neonatal HR monitoring. Further development of the HR algorithm, addition of oxygen saturation monitoring and evaluation during low perfusion states are underway.

ACKNOWLEDGEMENTS

Dr. Andrew Prayle helped to implement the modified Bland-Altman for multiple measurements. Thank you to all the families who kindly agreed to participate in this study.

ABBREVIATIONS

BT	Bluetooth
DCC	Delayed cord clamping
ECG	Electrocardiograph
ECS	Elective caesarean section
fhPPG	Forehead photoplethysmography
HR	Heart rate
IQR	Interquartile range
JIS T	Japanese Industrial Standard T
LOA	Limits of agreement
NICU	Neonatal Intensive Care Unit
PO	Pulse oximetry
PPG	Photoplethysmography
RMSE	Root mean square error
SD	Standard deviation

FUNDING

Innovate UK Biomedical Catalyst (MRC MC_PC_15012); Engineering and Physical Sciences Research Council (EP/K 503101/1 via Tioga Ltd PhD CASE award). Additional support by the Faculty of Engineering, University of Nottingham's Hermes Fellowship scheme (A1H361) and from the University of Nottingham EPSRC Impact Acceleration Award (EP/R511730/1 and RA45VJ).

CONFLICTS OF INTEREST

Following are shareholders in SurePulse Medical Ltd – Don Sharkey, Barrie Hayes-Gill, John Crowe, James Carpenter, Steve Morgan

James Carpenter is the chief executive officer for SurePulse Medical Ltd

Don Sharkey and Barrie Hayes-Gill are non-executive directors of SurePulse Medical Ltd

REFERENCES

1. Finer N, Rich W. Neonatal resuscitation for the preterm infant: evidence versus practice. *J Perinatol* 2010; 30 Suppl:S57-66.

2. Laptook AR, Salhab W, Bhaskar B. Admission temperature of low birth weight infants: predictors and associated morbidities. *Pediatrics* 2007; 119 (3):e643-9.

3. de Almeida MF, Guinsburg R, Sancho GA, Rosa IR, Lamy ZC, Martinez FE, et al. Hypothermia and early neonatal mortality in preterm infants. *J Pediatr* 2014; 164 (2):271-5.

4. Wyllie J, Perlman JM, Kattwinkel J, Wyckoff MH, Aziz K, Guinsburg R, et al. Part 7: Neonatal resuscitation: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Resuscitation* 2015; 95:e169-201.

5. Luong D, Cheung PY, Barrington KJ, Davis PG, Unrau J, Dakshinamurti S, et al. Cardiac arrest with pulseless electrical activity rhythm in newborn infants: a case series. *Arch Dis Child Fetal Neonatal Ed* 2019; 104:F572-4

6. Patel S, Cheung PY, Solevag AL, Barrington KJ, Kamlin COF, Davis PG, et al. Pulseless electrical activity: a misdiagnosed entity during asphyxia in newborn infants? *Arch Dis Child Fetal Neonatal Ed* 2019; 104 (2):F215-7.

7. Mann C, Ward C, Grubb M, Hayes-Gill B, Crowe J, Marlow N, et al. Marked variation in newborn resuscitation practice: a national survey in the UK. *Resuscitation* 2012; 83 5:607-11.

8. Kamlin CO, Dawson JA, O'Donnell CP, Morley CJ, Donath SM, Sekhon J, et al. Accuracy of pulse oximetry measurement of heart rate of newborn infants in the delivery room. *J Pediatr* 2008; 152 6:756-60.

9. van Vonderen JJ, Hooper SB, Kroese JK, Roest AA, Narayen IC, van Zwet EW, et al. Pulse Oximetry Measures a Lower Heart Rate at Birth Compared with Electrocardiography. *J Pediatr* 2015; 166 (1):49-53.

10. Murphy MC, De Angelis L, McCarthy LK, O'Donnell CPF. Randomised study comparing heart rate measurement in newly born infants using a monitor incorporating electrocardiogram and pulse oximeter versus pulse oximeter alone. *Arch Dis Child Fetal Neonatal Ed* 2019; 104: F547-50

11. Tarnow-Mordi W, Morris J, Kirby A, Robledo K, Askie L, Brown R, et al. Delayed versus Immediate Cord Clamping in Preterm Infants. *N Engl J Med* 2017; 377 (25):2445-55.

12. Manley BJ, Owen LS, Hooper SB, Jacobs SE, Cheong JLY, Doyle LW, et al. Towards evidence-based resuscitation of the newborn infant. *Lancet* 2017; 389 (10079):1639-48.

13. Grubb MR, Carpenter J, Crowe JA, Teoh J, Marlow N, Ward C, et al. Forehead reflectance photoplethysmography to monitor heart rate: preliminary results from neonatal patients. *Physiol Meas* 2014; 35 (5):881-93.

14. Fernandez M, Burns K, Calhoun B, George S, Martin B, Weaver C. Evaluation of a new pulse oximeter sensor. *Am J Crit Care* 2007; 16 (2):146-52.

15. Berkenbosch JW, Tobias JD. Comparison of a new forehead reflectance pulse oximeter sensor with a conventional digit sensor in pediatric patients. *Respir Care* 2006; 51 (7):726-31.

16. O'Donnell CP, Kamlin CO, Davis PG, Morley CJ. Feasibility of and delay in obtaining pulse oximetry during neonatal resuscitation. *J Pediatr* 2005; 147 (5):698-9.

17. O'Donnell CP, Kamlin CO, Davis PG, Morley CJ. Obtaining pulse oximetry data in neonates: a randomised crossover study of sensor application techniques. *Arch Dis Child Fetal Neonatal Ed* 2005; 90 (1):F84-5.

18. Louis D, Sundaram V, Kumar P. Pulse oximeter sensor application during neonatal resuscitation: a randomized controlled trial. *Pediatrics* 2014; 133 (3):476-82.

19. Japanese Industrial Standards JT. 分べん（娩）監視装置 Fetal monitors. Tokyo: Japanese Standards Association; 2005 (revised 2018)

20. Bustos R, Bejar R, Arroyave H, Jacomo AJ, Burghi M, Ramirez F, et al. Heart rate in fetuses and neonates in normal conditions and with mild depression. *J Perinat Med* 1975; 3 (3):172-9.

21. Cohen WR, Ommani S, Hassan S, Mirza FG, Solomon M, Brown R, et al. Accuracy and reliability of fetal heart rate monitoring using maternal abdominal surface electrodes. *Acta Obstet Gynecol Scand* 2012; 91 (11):1306-13.

22. Bland JM, Altman DG. Agreement between methods of measurement with multiple observations per individual. *J Biopharm Stat* 2007; 17 (4):571-82.

23. Altman DG, Bland JM. Measurement in medicine: the analysis of method comparison studies. *The Statistician* 1983:307-17.

24. Singh JK, Kamlin CO, Morley CJ, O'Donnell CP, Donath SM, Davis PG. Accuracy of pulse oximetry in assessing heart rate of infants in the neonatal intensive care unit. *J Paediatr Child Health* 2008; 44 (5):273-5.

25. Pickup L, Lang A, Shipley L, Henry C, Carpenter J, McCartney D, et al. Development of a Clinical Interface for a Novel Newborn Resuscitation Device: Human Factors Approach to Understanding Cognitive User Requirements. *JMIR Hum Factors* 2019; 6 2:e12055.

TABLES

Table 1. Patient demographics and baseline variables during NICU and elective caesarean section (ECS). Values are absolute numbers or median and interquartile range (IQR).

Demographic or Variable	NICU n=34	ECS n=18
Gestational age (weeks)	31+2 (28+5 - 35+5)	39+0 (38+6 - 39+3)
Age (days)	23 (10 - 39)	Birth
Birth Weight (g)	1460 (1019 - 2288)	3335 (2833 – 3561)
Male sex, n (%)	16 (47)	7 (39)
Ethnicity, n (%)		
White	32 (94)	14 (77)
Mixed white/Middle Eastern	1 (3)	-
Mixed white/Afro-Caribbean	-	1 (6)
Asian	-	1 (6)
Black	1 (3)	2 (11)
Resuscitation during study	-	2 (positive pressure mask ventilation)

Table 2. Bland-Altman limits of agreement (LOA), bias (fhPPG HR-ECG HR) and Root Mean Square of the Error (RMSE) expressed as medians from patient level data.

Measure	NICU (n=34)		ECS (n=18)	
	fhPPG	PO	fhPPG	PO
LOA (bpm)	-5.6, 4.9	-6.3, 6.2	-8.7, 7.7	-7.6, 7.1
Bias (bpm)	-0.6	-0.3	-0.5	-0.1
RMSE (bpm)	2.8	3.3	4.1	3.7

NICU=neonatal intensive care unit, ECS=elective caesarean section, fhPPG=forehead wireless cap PPG device, PO=pulse oximeter

FIGURE LEGENDS

Figure 1: Violin plots of the Root Mean Square of the Error (RMSE, median and interquartile range) for the wireless cap (fhPPG) device and the pulse oximeter (PO) in the neonatal intensive care unit (NICU, n=34) and at birth in the elective caesarean section (ECS) phase (n=18).

Figure 2. Linear regression of heart rate between pulse oximetry (PO) vs ECG (n=13935) and wireless cap (fhPPG) vs ECG (n=12939). Each data plot represents paired HR values between the devices.

Figure 3. Comparison of the Japanese Industrial Standard (JIS T) input signal with the wireless cap (fhPPG) algorithm output rate over simulated heart rate signals ranging from 25 to 250 bpm. Fluctuations are designed to simulate a number of heart rate changes observed in the newborn.

Figure 4. Linear regression plot of Japanese Industrial Standard (JIS T) input signal (n=1266) with the wireless cap (fhPPG) algorithm output (n=1264) rate. Each data plot represents paired HR values between the device and input signal.

The University of Nottingham
School of Medicine

Division of Child Health, Obstetrics and Gynaecology

Floor E, East Block
Queen's Medical Centre
Nottingham
NG7 2UH
Tel: +44 (0) 115 823 0612
Fax: +44 (0) 115 823 0626

Acta Paediatrica Response Letter SPAE-2020-0096

5th April 2020

Dear Editor,

We thank you and the Reviewers for their excellent comments on the manuscript entitled "Accurate neonatal heart rate monitoring using a new wireless, cap mounted device".

Please see our responses to the Reviewers comments below which we have highlighted any changes in the manuscript for ease of checking.

Please don't hesitate to contact us if you have any questions.

Yours faithfully,

D. Sharkey

Dr Don Sharkey
Associate Professor of Neonatal Medicine

Reviewer's comments and responses

Dear Editor and Reviewers,
Thank you for your comments. We have made the following changes:

1. Please rename the supplementary figure to Supplementary figure S1.
We have renamed the supplementary figure to Supplementary figure S1.

2. The revised manuscript states that "international guidelines recommend using the electrocardiogram (ECG)" (Introduction, sentence 3). ILCOR state that ECG may be used, rather than it should be used - a subtle but important distinction, that should be reflected. Otherwise, my comments have been addressed in the revised manuscript which reads very well.
Thank you. We have changed the manuscript so that the sentence now reads "Heart rate (HR) is the most sensitive predictor of the infant's clinical status and the efficacy of any interventions, and international guidelines suggest the electrocardiogram (ECG) may be used in the delivery room to monitor it".

TITLE

Accurate neonatal heart rate monitoring using a new wireless, cap mounted device

Caroline Henry[1], Lara Shipley[1], Carole Ward[1], Siavash Mirahmadi[2], Chong Liu[2], Steve Morgan[2], John Crowe[2], James Carpenter[3], Barrie Hayes-Gill[2], Don Sharkey[1]

[1]Division of Child Health, Obstetrics & Gynaecology, University of Nottingham, UK; [2]Faculty of Engineering, University of Nottingham, UK; [3]SurePulse Limited, Nottingham, UK

Short title: Neonatal heart rate monitoring

Corresponding author: Don Sharkey, Division of Child Health, Obstetrics & Gynaecology University of Nottingham, Queen's Medical Centre Campus, Derby Road, Nottingham, UK NG7 2UH. Tel 01158230602

ABSTRACT

Aim: A device for newborn heart rate (HR) monitoring at birth that is compatible with delayed cord clamping and minimises hypothermia risk could have advantages over current approaches. We evaluated a wireless, cap-mounted device (fhPPG) for monitoring neonatal HR. ***Methods***: 52 infants on the Neonatal Intensive Care Unit (NICU) and immediately following birth by elective caesarean section (ECS) were recruited. HR was monitored by electrocardiogram (ECG), pulse oximetry (PO) and the fhPPG device. Success rate, accuracy and time to output HR were compared with ECG as the gold standard. Standardised simulated data assessed the fhPPG algorithm accuracy. ***Results***: Compared to ECG HR, the median bias (and 95% limits of agreement) for the NICU were fhPPG -0.6 (-5.6, 4.9) vs PO -0.3 (-6.3, 6.2) bpm, and ECS phase fhPPG -0.5 (-8.7, 7.7) vs PO -0.1 (-7.6, 7.1) bpm. In both settings, fhPPG and PO correlated with paired-ECG HRs (both R^2=0.89). The fhPPG HR algorithm during simulations demonstrated a near-linear correlation (n=1266, R^2=0.99).

Conclusion: Monitoring infants in the NICU and following ECS using a wireless, cap mounted device provides accurate HR measurements. This alternative approach could confer advantages compared with current methods of HR assessment and warrants further evaluation at birth.

Keywords

Heart Rate; Infant, Newborn; Photoplethysmography; Resuscitation; Technologies, wireless

KEY NOTES

- Wireless continuous heart rate (HR) monitoring of infants using a cap (fhPPG) could be beneficial during delayed cord clamping
- Using electrocardiography as a gold standard, the fhPPG had similar bias and 95% limits of agreement as pulse oximetry on the Neonatal Intensive Care Unit and immediately after birth by caesarean section. There was close correlation to paired-ECG HRs
- Using standardised simulated HR data, the fhPPG algorithm demonstrated near-linear correlation
- The fhPPG is an accurate alternative to current methods of HR monitoring

INTRODUCTION

Approximately 10% of newborns require assistance at birth to establish breathing with 3% needing more sustained stabilisation or resuscitation.(1) Preterm infants often require more advanced stabilisation or resuscitation whilst avoiding hypothermia, known to increase mortality.(2, 3) Heart rate (HR) is the most sensitive predictor of the infant's clinical status and the efficacy of any interventions, and international guidelines suggest the electrocardiogram (ECG) may be used in the delivery room to monitor it.(4) However, electrode application can be difficult, ECG monitors are not always available and electrical cardiac activity may not always equate to effective cardiac output.(5, 6) Pulse oximetry (PO) is widely used on neonatal intensive care units (NICUs) but uptake in the delivery room is not universal (7) potentially because of the delay of a few minutes to obtain a reliable HR after birth due to poor peripheral perfusion and motion.(8) This could explain why PO underestimates HR when compared to ECG during the first minutes of life.(9, 10)

Delayed cord clamping (DCC) for term infants is widely practiced and could become more common for preterm infants but there is a need to better monitor these babies during this transition to maximise the benefits of DCC whilst avoiding any adverse effects of delayed resuscitation.(11, 12) Maximising placental transfusion requires the attending team to be confident of the baby's condition including an acceptable HR and avoidance of hypothermia. A non-intrusive, wireless, easy to apply HR monitoring system, which avoids the risk of hypothermia, could be advantageous in this setting.

We have previously described a prototype wired, forehead mounted sensor studied in NICU patients that utilises reflectance mode green light photoplethysmography (PPG) to measure HR.(13) This has the advantages that this wavelength of light (525 nm) is optimised for reflection mode detection of blood flow and captures this at the forehead where brain perfusion shares arterial pathways via the carotid artery and so is less susceptible to poor peripheral perfusion.(14, 15) This original device was held in place on the forehead by a spun bond laminate headband and successfully demonstrated that HR measurement by this method was feasible but had a Bland-Altman limit of agreement (LOA) of up to ±12bpm. In addition, it was not compatible with current neonatal care due to its inability to accommodate endotracheal tube and CPAP attachments. Furthermore, the relatively large sensor (22 mm diameter), large electronic circuit boards and the presence of cumbersome wiring were less suited for bedside stabilisation of preterm infants during DCC.

This device has now been substantially modified (Supplemental video and images) in terms of its practicality and several major modifications have taken place including:

i) A T-shape cap compatible with respiratory equipment fittings
ii) A miniaturised and ruggedized sensor (10 mm diameter)
iii) Bluetooth (BT) wireless connection removing the need for trailing wires

The primary aim of this study was to assess, via a clinical trial, the accuracy and reliability of this new cap mounted newborn HR device the SurePulse VS (fhPPG) (SurePulse Medical Ltd, Nottingham, UK). The study was designed to satisfy the regulatory requirements of the CE Medical Devices Directive 93/42 and its 2007 amendment for measuring HR compared to PO, with ECG as a gold standard. A secondary aim was to investigate acquisition time.

MATERIALS AND METHODS

Study Population

This prospective observational study was conducted at the Nottingham University Hospitals NHS Trust, UK following ethical approval (NHS Health Research Authority Yorkshire & The Humber – Sheffield Research Ethics Committee 15/YH/0522). Informed parental consent was obtained prior to infants being enrolled in the study and evaluations were performed in the NICU and on babies born by elective caesarean section (ECS). For the NICU phase, infants were included if they were >22 weeks gestation, required HR monitoring and were deemed clinically stable by the attending team. Inclusion criteria for the ECS phase were infants ≥37 weeks gestation with no obvious requirement for resuscitation, based on antenatal history, and delivered by planned caesarean section.

Study Design

There were two phases to this study, the NICU and ECS. On the NICU, an appropriately sized fhPPG cap was fitted to the infant's head and connected wirelessly to a bespoke synchronised data-logging system via the inbuilt wireless BT module. As part of their routine care, infants had 3 neonatal ECG monitoring electrodes (PD50-F4C, SKINTACT, Leonhard Lang GmbH, Innsbruck, Austria) attached and connected to a CARESCAPE Monitor B450 (General Electric Healthcare, Illinois, United States) with Masimo SET® for SpO2 (Masimo, California, United States). A transmission mode PO sensor (LNCS Neo, Masimo, California, United States) was attached to the wrist of the right hand and connected to the same monitor. An in-house designed system using LabVIEW 2014 (National Instruments, Texas, United States) simultaneously collected synchronised data from all devices and displayed waveforms from each device in real time on a laptop (Lenovo Y50 20378, Lenovo Group Ltd, Hong Kong). In keeping with normal practice, if any device presented a poor signal output the electrodes or optical sensors (head or wrist) were repositioned. Up to 30 minutes of raw physiological data were collected with the infant in their cot or incubator.

During the ECS phase, the same monitoring system described above was deployed. Following birth, the baby was shown to parents before being placed on the resuscitaire. All monitoring equipment was attached in the same sequence for each patient by the research team. The fhPPG cap was fitted, ECG leads attached and a PO sensor attached to the wrist of the right hand(16-18) and raw data collected for up to 20 minutes.

The B450 monitor generates HR data which provides ECG and PO values every 5 seconds. All fhPPG HR data extracted were averaged over the same 5 second window for direct comparison.

Slow and rapidly changing HRs can be unpredictable in the NICU and ECS settings. To ensure the fhPPG HR algorithm can effectively extract a wide range of rapidly changing HRs, as experienced during newborn care, we subjected the algorithm to simulated HR data covering

25 to 250 bpm using the Japanese Industrial Standard (JIS T 1303:2005, revised 2018).(19) Although the JIS T is designed for testing fetal heart rate monitors, it appropriately models newborns as the HR baseline and variation are similar to those of the fetus.(20) A simulated PPG signal was input across the JIS T range of HRs, the algorithm's performance tracked and linear regression applied to evaluate the overall performance.

Data Analysis

HR data from either PO or fhPPG were excluded if there was no ECG (the gold standard) HR comparator, a protocol violation occurred or a device was detached from the patient. To ensure good quality gold standard data, erroneous ECG HR data, as previously observed,(13) were excluded if there was no discernible QRS complexes or there had been an algorithm drop out. If the ECG HR value deviated by >20% from the other test devices (PO and/or fhPPG), the RR interval on the raw ECG trace corresponding to that time point was manually checked and excluded if the manual ECG HR check deviated from the reported ECG HR by >10%.

The success rate was calculated as the percentage of time during which the device in question was attached to the patient and reporting a HR once all three devices were simultaneously outputting a valid HR.

Comparison of the HR accuracy (fhPPG and PO) with the gold standard (ECG) utilised three methods: 1) Positive Percent Agreement (PPA) which is the percentage of time the test device generated a valid HR within 10% of the paired ECG HR,(21) 2) modified Bland-Altman plots to correct for multiple measurements and it's limits of agreement (LOA),(22, 23) and 3) Root-Mean-Square Error (RMSE) calculated between paired HRs (fhPPG vs ECG, and PO vs ECG). HR output time for each device is the time taken from completion of its attachment to the display of a HR.

Analyses were performed using GraphPad Prism 7.01 (GraphPad, California, USA). Continuous variables were tested for normality using the Kolmogorov-Smirnov test. Data were presented as mean (SD), median (range), or median (IQR) where appropriate. Non-parametric data were compared using the Wilcoxon signed rank test and between groups were compared using Friedman's test with a Dunn's correction for multiple comparisons. The study was registered at Clinicaltrials.gov NCT 02701920.

RESULTS

A convenience sample of 60 infants were recruited (NICU = 40, ECS = 20) when researchers were available. Six infants were excluded from the NICU phase and two from the ECS phase due to ECG data not being stored or corrupted leading to data loss and misalignment. The patient demographics can be seen in Table 1.

Success Rate

During the NICU phase, the median ECG success rate was 100% (IQR, 100-100, n=12967), PO was 100% (IQR, 99.1-100, n=12688) and fhPPG was 98.7% (IQR, 93.9-100, n=11501). During the ECS phase, the median ECG success rate was 96.2% (IQR, 91.9-100, n=2039), PO was 98.1% (IQR, 89.5-100, n=1903) and fhPPG was 94.1% (IQR, 84.1- 98.4, n=1805).

Accuracy of devices

During the NICU phase, the median PPAs were similar for fhPPG (99.6%; IQR 99.0-100, n=11353) and PO (99.4%; IQR 99.0-100, n=12249). During the ECS phase, the median PPAs were again similar for fhPPG (98.6%; IQR 96.4-100, n=1584) and PO (98.7%; IQR 97.2-100, n=1684). Device comparison to the gold standard was also determined using both Bland-Altman plots (Table 2) and RMSE (Table 2 and Figure 1).

Linear regression of all pooled paired HRs demonstrated PO and fhPPG had similar goodness of fit with both having an R^2=0.89 (Figure 2). In five babies, the ECG measured a HR<100 bpm. For these, there were 23 paired values with the PO of which two reported a HR>100 bpm and for the fhPPG there were 13 paired values with two reporting a HR>100 bpm, on both occasions the fhPPG output was identified as a poor signal triggering a warning to the user.

Algorithm simulation

Simulated PPG data were applied as described across a range of HRs and with varying rates of change as defined by JIS T (Figure 3). The fhPPG algorithm demonstrated excellent correlation with the simulated HR (Figure 4).

Heart rate output time

Median time for HR output was similar for all three devices during the ECS phase. For ECG this was 24.5s (IQR 14.2-31.2), fhPPG 35.5s (IQR 16.7-53.7) and PO 24.5s (IQR 13.5-53.5) with no statistical significance between any of the devices.

DISCUSSION

We aimed to establish the accuracy and reliability of a new wireless, cap mounted HR monitoring device (fhPPG) in the neonatal setting and compare this to the HR obtained from PO. The fhPPG device provided accurate and reliable HR data compared to current predicate devices generating a median RMSE of 2.8 bpm compared to 3.3 bpm for PO in the NICU. In the ECS phase at birth, median RMSE values of 4.1 bpm and 3.7 bpm were obtained for the fhPPG and PO devices respectively. Time to output a HR after placement in the delivery room was similar across all three devices.

All devices provided similar success rates when outputting a HR. During the NICU phase, the fhPPG device had fewer data points because of the requirement to remove and replace the device for safety checks as required by the Ethics panel. The high ECG success rate reflects the use of electrodes that were already in place for normal neonatal care and, unlike the fhPPG device, were not removed and re-sited for safety and acquisition time purposes.

Accuracy, as measured by PPA, Bland-Altman and RMSE demonstrated the fhPPG device was similar to the PO in both settings. The measures of variance for each of these measures were within clinically acceptable limits, both optical devices providing accurate data when compared to the ECG that detects electrical activity. This requires the algorithms to respond in a timely fashion to rapid changes in HR, a key requirement of any device in these settings. For PO in the NICU, Singh et al (2008) had demonstrated the Bland-Altman LOA of ±12 bpm.(24) In our study, the PO performed much better in the NICU and ECS groups. For the new fhPPG device, accuracy in the NICU has improved to approximately ±5 bpm from the previous iteration with LOAs of up to ±12 bpm.(13) This improved accuracy remained for the fhPPG device during the ECS phase with LOAs of approximately ±8 bpm. PO has been studied in the delivery room across a range of gestational ages. Kamlin et al's study were mostly mature infants, with a mean gestational age of 35 weeks, and the majority (65%) did not require any intervention. The Bland-Altman demonstrated a mean difference of -2 bpm and LOA of ±26 bpm. The results for both PO and fhPPG in the present study were significantly better although the groups were not entirely comparable with only infants ≥37 weeks gestation recruited at birth in the ECS group. The additional measures of HR accuracy also add confidence that the fhPPG device performs as well as current devices with a PPA of approximately 99%, in the NICU and ECS phase, and an RMSE 3-4 bpm. Furthermore, both the PO and fhPPG devices produced high correlations with an R^2=0.89 for goodness-of-fit compared to ECG HR. For the ECS phase, these data are reassuring given the vigorous nature of the babies at birth and the significant motion artefact introduced.

It is essential that any newborn HR monitoring device is able to detect low rates, particularly those below 100bpm. The majority of babies in this study were stable with limited HR variability so limiting the number of HRs <100bpm. Use of the JIS T methodology allowed us to test the software algorithm to rapidly changing simulated HRs across the typical newborn range. The fhPPG algorithm was able to track the HRs quickly and accurately with an R^2=0.994. This strong correlation supports the accuracy of the device's software based on simulation data but the whole system requires real-world evaluation with infants undergoing resuscitation or stabilisation.

The secondary aim of this study was to explore the acquisition time of the new device, as it is essential for fast delivery of information to the attending team to allow correct management of the baby. Output of the HR at birth for all devices was similar although more babies in the study would be required to confirm this persisted or identify any differences. ECG measures electrical activity and has been shown to acquire a HR quicker than pulse oximeters, possibly reflecting delayed acquisition from early cutaneous perfusion increasing in the first few minutes of life. The fhPPG device uses green light to measure HR, but also has red and infrared light that are optimised for oxygen saturation measurement and used by POs to measure HR. Green light is better suited to detecting pulsatile blood flow (13) so potentially optimising HR estimation particularly during low perfusion states. The sequence of device attachment after birth was fhPPG, ECG and PO respectively, potentially disadvantaging the fhPPG device as it was placed earlier during the transition period. Whilst fast detection of electrical activity of the heart is useful, when cardiac output is poor or non-existent(5, 6) there could be advantages to having a parallel optical sensor that is able to detect blood flow and hence confirm the electrical activity is associated with cardiac output. Any potential benefits of a centrally placed, green light optical sensor, i.e. fhPPG which detects blood flow from the forehead sharing a common central arterial blood supply to the brain, compared to a peripherally sited transmission mode device requires further evaluation in larger number of patients including preterm infants.

The main limitation of the present study is the low number of HRs below 100, reflecting the nature of the population who were stable NICU patients or ECS term babies born following uncomplicated pregnancies. There were fewer paired ECG and fhPPG values <100bpm, compared to the PO, due to sensor repositioning as the signal had been identified as poor. We mitigated against low HRs by using the JIS T methodology fully exercising the software algorithm to create HR values over the range 25-250 bpm confirming successful algorithm functionality. However, additional studies are required to establish this in compromised newborns, especially those with HRs<100 bpm, where the HR variability changes frequently and a larger number of preterm infants.

CONCLUSION

With the increasing use of DCC the development of a wireless, continuous HR monitor that aligns with the normal care pathway, including placement of a cap with attachment for respiratory equipment, could better support transitioning of newborn babies and audit interventions.(25) Confidence in such a device could allow monitoring of the newborn and aid decisions around when to clamp the cord and instigate any stabilisation or additional resuscitation steps. fhPPG operates in reflectance mode allowing detection of a PPG signal on many parts of the body. The forehead allows inclusion in a cap, normally applied to keep the baby warm, and could potentially improve reliability during low perfusion states with a shared carotid artery blood supply to the brain.(13) The wireless design avoids multiple trailing wires that could become accidentally detached during bedside care with DCC. This device provides healthcare professionals with an accurate alternative to current neonatal HR monitoring. Further development of the HR algorithm, addition of oxygen saturation monitoring and evaluation during low perfusion states are underway.

ACKNOWLEDGEMENTS

Dr. Andrew Prayle helped to implement the modified Bland-Altman for multiple measurements.

Thank you to all the families who kindly agreed to participate in this study.

ABBREVIATIONS

BT	Bluetooth
DCC	Delayed cord clamping
ECG	Electrocardiograph
ECS	Elective caesarean section
fhPPG	Forehead photoplethysmography
HR	Heart rate
IQR	Interquartile range
JIS T	Japanese Industrial Standard T
LOA	Limits of agreement
NICU	Neonatal Intensive Care Unit
PO	Pulse oximetry
PPG	Photoplethysmography
RMSE	Root mean square error
SD	Standard deviation

FUNDING

Innovate UK Biomedical Catalyst (MRC MC_PC_15012); Engineering and Physical Sciences Research Council (EP/K 503101/1 via Tioga Ltd PhD CASE award). Additional support by the Faculty of Engineering, University of Nottingham's Hermes Fellowship scheme (A1H361) and from the University of Nottingham EPSRC Impact Acceleration Award (EP/R511730/1 and RA45VJ).

CONFLICTS OF INTEREST

Following are shareholders in SurePulse Medical Ltd – Don Sharkey, Barrie Hayes-Gill, John Crowe, James Carpenter, Steve Morgan

James Carpenter is the chief executive officer for SurePulse Medical Ltd

Don Sharkey and Barrie Hayes-Gill are non-executive directors of SurePulse Medical Ltd

REFERENCES

1. Finer N, Rich W. Neonatal resuscitation for the preterm infant: evidence versus practice. *J Perinatol* 2010; 30 Suppl:S57-66.
2. Laptook AR, Salhab W, Bhaskar B. Admission temperature of low birth weight infants: predictors and associated morbidities. *Pediatrics* 2007; 119 (3):e643-9.
3. de Almeida MF, Guinsburg R, Sancho GA, Rosa IR, Lamy ZC, Martinez FE, et al. Hypothermia and early neonatal mortality in preterm infants. *J Pediatr* 2014; 164 (2):271-5.
4. Wyllie J, Perlman JM, Kattwinkel J, Wyckoff MH, Aziz K, Guinsburg R, et al. Part 7: Neonatal resuscitation: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations. *Resuscitation* 2015; 95:e169-201.
5. Luong D, Cheung PY, Barrington KJ, Davis PG, Unrau J, Dakshinamurti S, et al. Cardiac arrest with pulseless electrical activity rhythm in newborn infants: a case series. *Arch Dis Child Fetal Neonatal Ed* 2019; 104:F572-4
6. Patel S, Cheung PY, Solevag AL, Barrington KJ, Kamlin COF, Davis PG, et al. Pulseless electrical activity: a misdiagnosed entity during asphyxia in newborn infants? *Arch Dis Child Fetal Neonatal Ed* 2019; 104 (2):F215-7.
7. Mann C, Ward C, Grubb M, Hayes-Gill B, Crowe J, Marlow N, et al. Marked variation in newborn resuscitation practice: a national survey in the UK. *Resuscitation* 2012; 83 5:607-11.
8. Kamlin CO, Dawson JA, O'Donnell CP, Morley CJ, Donath SM, Sekhon J, et al. Accuracy of pulse oximetry measurement of heart rate of newborn infants in the delivery room. *J Pediatr* 2008; 152 6:756-60.
9. van Vonderen JJ, Hooper SB, Kroese JK, Roest AA, Narayen IC, van Zwet EW, et al. Pulse Oximetry Measures a Lower Heart Rate at Birth Compared with Electrocardiography. *J Pediatr* 2015; 166 (1):49-53.
10. Murphy MC, De Angelis L, McCarthy LK, O'Donnell CPF. Randomised study comparing heart rate measurement in newly born infants using a monitor incorporating electrocardiogram and pulse oximeter versus pulse oximeter alone. *Arch Dis Child Fetal Neonatal Ed* 2019; 104: F547-50
11. Tarnow-Mordi W, Morris J, Kirby A, Robledo K, Askie L, Brown R, et al. Delayed versus Immediate Cord Clamping in Preterm Infants. *N Engl J Med* 2017; 377 (25):2445-55.

12. Manley BJ, Owen LS, Hooper SB, Jacobs SE, Cheong JLY, Doyle LW, et al. Towards evidence-based resuscitation of the newborn infant. *Lancet* 2017; 389 (10079):1639-48.

13. Grubb MR, Carpenter J, Crowe JA, Teoh J, Marlow N, Ward C, et al. Forehead reflectance photoplethysmography to monitor heart rate: preliminary results from neonatal patients. *Physiol Meas* 2014; 35 (5):881-93.

14. Fernandez M, Burns K, Calhoun B, George S, Martin B, Weaver C. Evaluation of a new pulse oximeter sensor. *Am J Crit Care* 2007; 16 (2):146-52.

15. Berkenbosch JW, Tobias JD. Comparison of a new forehead reflectance pulse oximeter sensor with a conventional digit sensor in pediatric patients. *Respir Care* 2006; 51 (7):726-31.

16. O'Donnell CP, Kamlin CO, Davis PG, Morley CJ. Feasibility of and delay in obtaining pulse oximetry during neonatal resuscitation. *J Pediatr* 2005; 147 (5):698-9.

17. O'Donnell CP, Kamlin CO, Davis PG, Morley CJ. Obtaining pulse oximetry data in neonates: a randomised crossover study of sensor application techniques. *Arch Dis Child Fetal Neonatal Ed* 2005; 90 (1):F84-5.

18. Louis D, Sundaram V, Kumar P. Pulse oximeter sensor application during neonatal resuscitation: a randomized controlled trial. *Pediatrics* 2014; 133 (3):476-82.

19. Japanese Industrial Standards JT. 分べん（娩）監視装置 Fetal monitors. Tokyo: Japanese Standards Association; 2005 (revised 2018)

20. Bustos R, Bejar R, Arroyave H, Jacomo AJ, Burghi M, Ramirez F, et al. Heart rate in fetuses and neonates in normal conditions and with mild depression. *J Perinat Med* 1975; 3 (3):172-9.

21. Cohen WR, Ommani S, Hassan S, Mirza FG, Solomon M, Brown R, et al. Accuracy and reliability of fetal heart rate monitoring using maternal abdominal surface electrodes. *Acta Obstet Gynecol Scand* 2012; 91 (11):1306-13.

22. Bland JM, Altman DG. Agreement between methods of measurement with multiple observations per individual. *J Biopharm Stat* 2007; 17 (4):571-82.

23. Altman DG, Bland JM. Measurement in medicine: the analysis of method comparison studies. *The Statistician* 1983:307-17.

24. Singh JK, Kamlin CO, Morley CJ, O'Donnell CP, Donath SM, Davis PG. Accuracy of pulse oximetry in assessing heart rate of infants in the neonatal intensive care unit. *J Paediatr Child Health* 2008; 44 (5):273-5.

25. Pickup L, Lang A, Shipley L, Henry C, Carpenter J, McCartney D, et al. Development of a Clinical Interface for a Novel Newborn Resuscitation Device: Human Factors Approach to Understanding Cognitive User Requirements. *JMIR Hum Factors* 2019; 6 2:e12055.

Table 1. Patient demographics and baseline variables during NICU and elective caesarean section (ECS). Values are absolute numbers or median and interquartile range (IQR).

Demographic or Variable	NICU n=34	ECS n=18
Gestational age (weeks)	31+2 (28+5 - 35+5)	39+0 (38+6 - 39+3)
Age (days)	23 (10 - 39)	Birth
Birth Weight (g)	1460 (1019 - 2288)	3335 (2833 – 3561)
Male sex, n (%)	16 (47)	7 (39)
Ethnicity, n (%)		
White	32 (94)	14 (77)
Mixed white/Middle Eastern	1 (3)	-
Mixed white/Afro-Caribbean	-	1 (6)
Asian	-	1 (6)
Black	1 (3)	2 (11)
Resuscitation during study	-	2 (positive pressure mask ventilation)

Table 2. Bland-Altman limits of agreement (LOA), bias (fhPPG HR-ECG HR) and Root Mean Square of the Error (RMSE) expressed as medians from patient level data.

Measure	NICU (n=34)		ECS (n=18)	
	fhPPG	**PO**	**fhPPG**	**PO**
LOA (bpm)	-5.6, 4.9	-6.3, 6.2	-8.7, 7.7	-7.6, 7.1
Bias (bpm)	-0.6	-0.3	-0.5	-0.1
RMSE (bpm)	2.8	3.3	4.1	3.7

NICU=neonatal intensive care unit, ECS=elective caesarean section, fhPPG=forehead wireless cap PPG device, PO=pulse oximeter

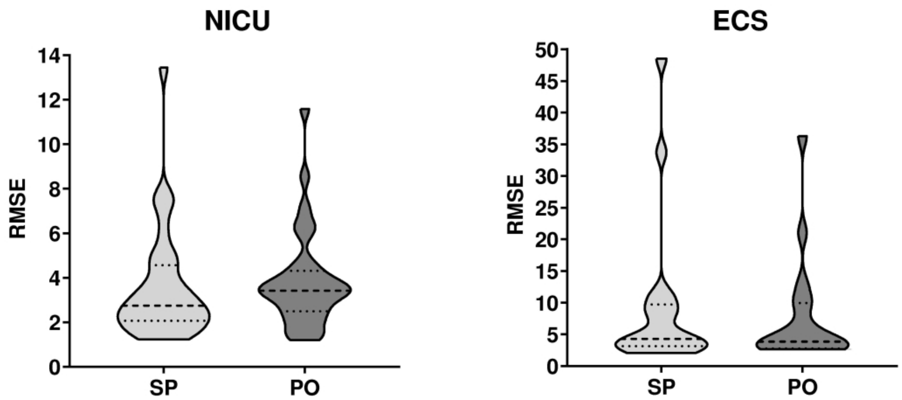


Figure 1: Violin plots of the Root Mean Square of the Error (RMSE, median and interquartile range) for the wireless cap (fhPPG) device and the pulse oximeter (PO) in the neonatal intensive care unit (NICU, n=34) and at birth in the elective caesarean section (ECS) phase (n=18).

180x78mm (600 x 600 DPI)

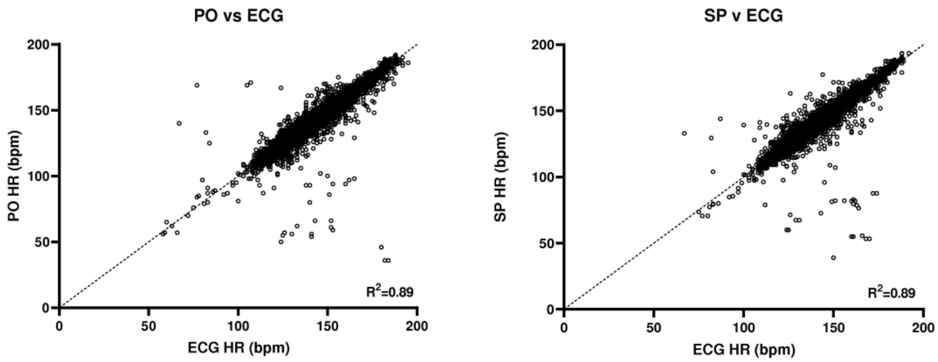


Figure 2. Linear regression of heart rate between pulse oximetry (PO) vs ECG (n=13935) and wireless cap (fhPPG) vs ECG (n=12939). Each data plot represents paired HR values between the devices.

180x72mm (600 x 600 DPI)

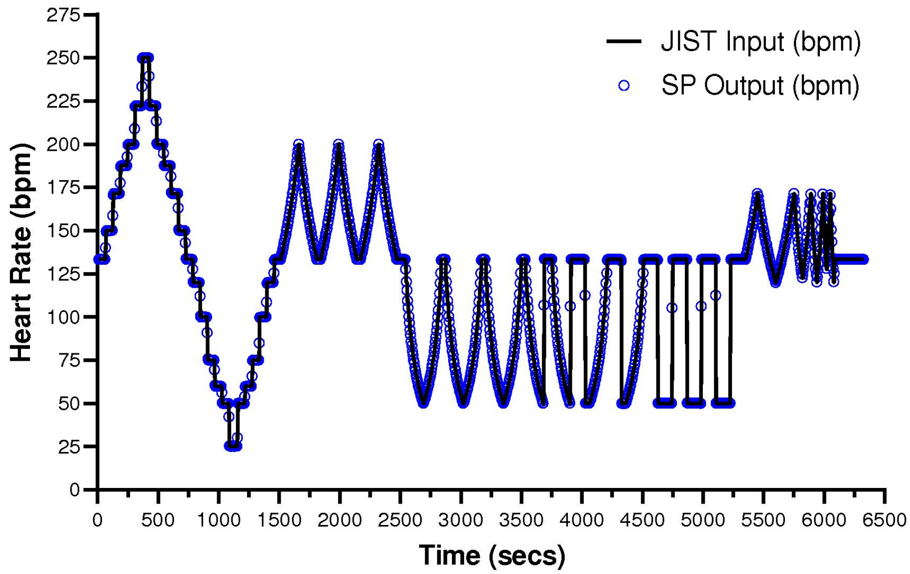


Figure 3. Comparison of the Japanese Industrial Standard (JIS T) input signal with the wireless cap (fhPPG) algorithm output rate over simulated heart rate signals ranging from 25 to 250 bpm. Fluctuations are designed to simulate a number of heart rate changes observed in the newborn.

80x52mm (600 x 600 DPI)

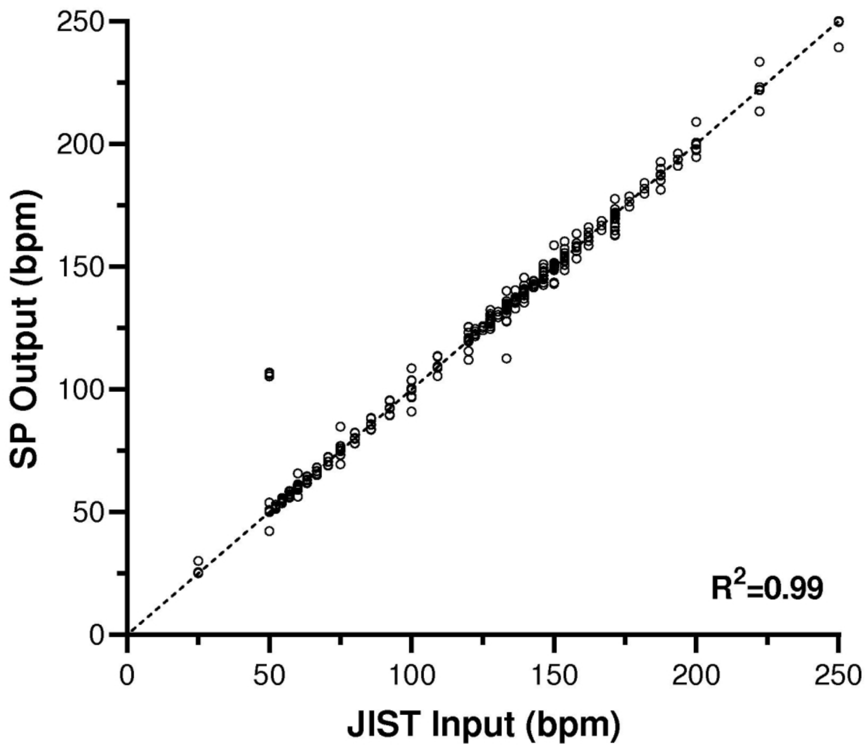
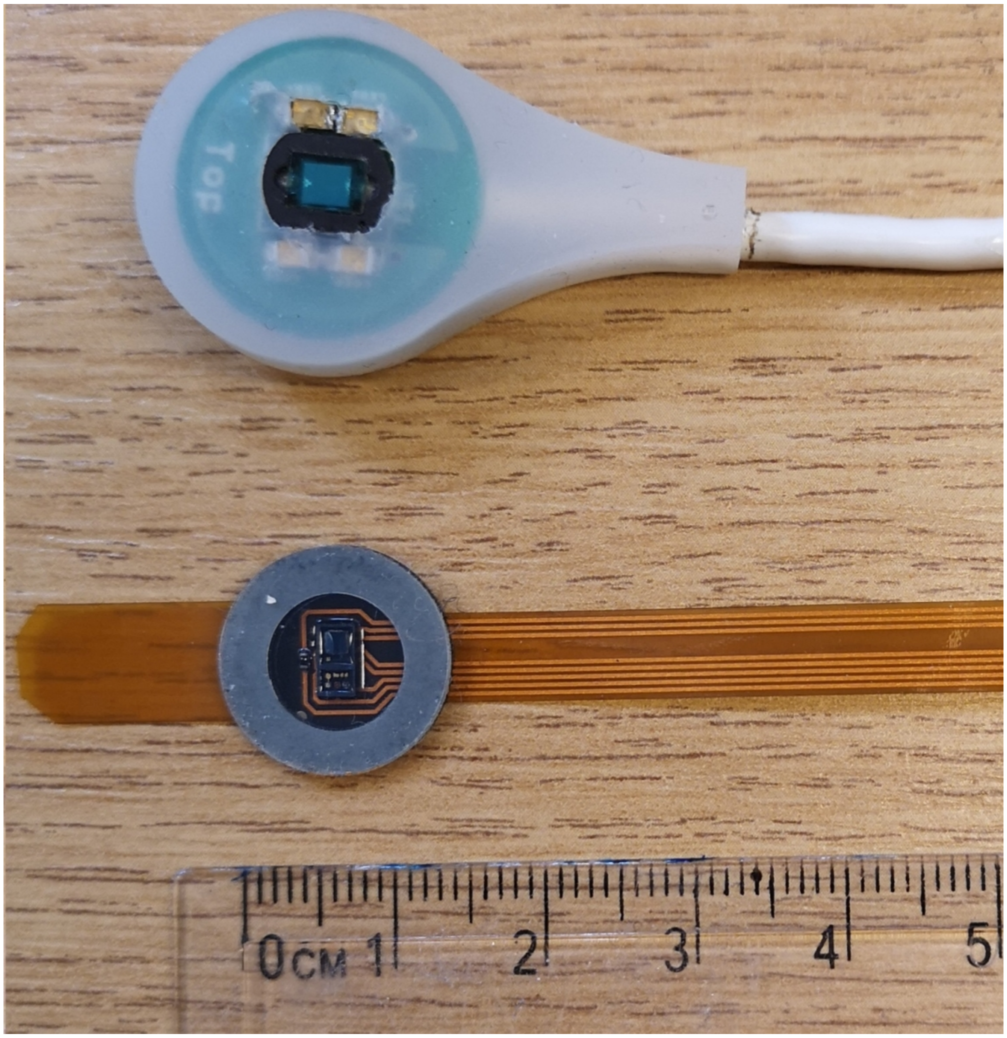


Figure 4. Linear regression plot of Japanese Industrial Standard (JIS T) input signal (n=1266) with the wireless cap (fhPPG) algorithm output (n=1264) rate. Each data plot represents paired HR values between the device and input signal.

80x67mm (600 x 600 DPI)

Supplementary figure S1: Application of the forehead photoplethysmography (fhPPG) device to a newborn baby. The sensor sits above the right eyebrow.



523x539mm (72 x 72 DPI)